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Regional variation in surgery for pancreatic cancer in Denmark 2011-2015

Kasper Wennervaldt¹, Anne Mette Kejs¹, Henriette Lipczak¹, Paul Bartels², Michael Borre^{3,4}, Claus Wilki Frstrup⁵ & Henrik Kehlet⁶

ABSTRACT

INTRODUCTION: Surgical treatment for pancreatic cancer carries a high risk of both morbidity and mortality. Even so, it remains the best curative treatment option. In Denmark, pancreatic surgery has been extensively centralised since the millennium, but the effect of this centralisation on patient outcome has not been evaluated. This study describes regional variation within pancreatic surgery on a malignant indication, focusing on production volume, length of stay, readmission rates and mortality.

METHODS: This is a retrospective cohort study of all patients with pancreatic cancer who underwent surgical treatment in Denmark from 2011 to 2015. We obtained data from the Danish National Patient Registry and the National Pathology Data Bank on length of stay, transfers, mortality (both short and long term), age, co-morbidity, and disease stage.

RESULTS: Four hospital units performed a total of 691 surgical procedures (476 pancreaticoduodenectomies) in the study period. Production volume varied considerably across units with two units accounting for nearly 80% of surgery performed. Data revealed variation on rates of transfers and readmissions as well as disease stage and mortality (both short and long term).

CONCLUSIONS: DATA suggest that mortality is linked to production volume as well as disease stage, but the small data quantity impedes rigorous statistical analysis. Further studies on the observed associations are required.

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To provide the best possible cancer care in Denmark, the government and the Danish Regions introduced nationally integrated cancer patient pathways in 2007. The aim was to shorten waiting times and increase survival rates by implementing organisational and clinical standards for the diagnostics and treatment of cancer. This implementation has led to a significant reduction in waiting time, which potentially could contribute to an increase in the overall survival [1], but the direct causality has yet to be determined. Surgery is an essential part of cancer treatment. However, little knowledge about the regional variation related to this intervention is available.

A collaborative of representatives from the Danish Cancer Society, the Danish Multidisciplinary Cancer

Groups, the Danish Regions and the Danish Clinical Registries formed a partnership to analyse regional variation in quality and patient safety in Denmark and ideally to propose improvement initiatives within surgical cancer treatment in selected areas. The present study on pancreatic cancer surgery is part of that work.

Surgery is the cornerstone in the treatment of pancreatic cancer with a curative intent, but even in combination with medical oncology the disease carries a high risk of morbidity and mortality. The past two decades have seen a rise in both incidence and mortality of pancreatic cancer in Denmark [2]. In the same period, pancreatic surgery has been extensively centralised from 12 performing units in 2001 to five in 2008 and four at the moment. The reorganisation was, in part, based on findings from two earlier studies that documented a considerable variation in hospitalisation, readmissions and mortality [3, 4]. The reduction of the number of performing units to the present level has not been formally evaluated, and the effect on patient outcomes remains unknown.

This study aims to describe regional variation within pancreatic surgery in Denmark focusing on length of stay, readmission rates and mortality.

METHODS

We performed a retrospective cohort study of all patients in Denmark with pancreatic cancer (International Classification of Diseases, 10th revision (ICD10): C25.1-3 and C25.5-9) who underwent one of four types of elective cancer resections: pancreaticoduodenectomy (PD), distal, total and local pancreaticoduodenal resection

(KJLC 00/10/20/30/40/50/60/96). Neuroendocrine malignancies (C25.4) as well as malignancies of the small intestines (C17) and the bile duct (C24) were excluded. Procedures classified as experimental, part of a protocol or performed outside the four hospitals approved for cancer surgery by the Danish Health Authority were likewise excluded.

We obtained data from the Danish National Patient Registry (DNPR) and the National Pathology Data Bank (Patobank) for the period from 1 January 2011 to 30 June 2015. The DNPR was used to create entry records that were then cross-referenced to Patobank to obtain supplemental data on Tumour-Node-Metastasis (TNM)

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using SNOMED codes for pancreas, ductus-, caput-, corpus-, cauda pancreaticus, and papilla et ampulla variteri (SNOMED T5900, T59010, T59100, T59200, T59300, and T58700). The wider search in Patobank was chosen not to overlook any cases while allowing the ICD-10 codes to define the population.

We collected data on date of admission and surgery, transfers and discharges, hospital and unit identity, type of hospitalisation, surgical procedure, primary and secondary diagnosis, age, co-morbidity, and TNM.

Descriptive statistics

Three main indicators were defined and calculated: length of stay, readmissions, and mortality. These indi-

cators were used for each procedure, at both a national and a regional (performing units) level.

Length-of-stay comprises:

- ▶ Surgical: number of days from the first admission day at the surgical unit until discharge.
- ▶ Total: number of days from the first admission day at the surgical unit until complete discharge including any transfer to units within the hospital or other hospitals.
- ▶ Complex admissions: number of admissions in which the patient is transferred to another unit or hospital.
- ▶ The subsequent length of stay: number of days spent at receiving unit or hospital after transfer (complex admissions).

Readmissions include:

- ▶ Readmissions: number of any unplanned readmission to any hospital in Denmark within 30 days from discharge from any hospital, following one of the defined procedures. The indicator included all diagnoses except for trauma.

Mortality covers:

- ▶ Hospital mortality: number of deaths within primary hospitalisation until one year after the date of the procedure, including death after transfer (complex admissions).
- ▶ 30-day mortality: number of deaths until 30 days after the date of the procedure.
- ▶ 90-day mortality: number of deaths until 90 days after the date of the procedure.
- ▶ 180-day mortality: number of deaths until 180 days after the date of the procedure.
- ▶ One-year mortality: number of deaths until 365 days after the date of the procedure.

By dividing the number of deaths by the total number of procedures, rates were calculated for all the mortality indicators.

Burden of disease, age, and co-morbidity served to adjust for case mix on a national level and for each of the performing units, as follows:

- ▶ Disease stage (DS): the most comprehensive TNM (both pre- and postoperative) extracted from TNM data limited to 90 days before and after the date of surgery.
- ▶ Burden of disease (BOD): percentage of patients with disease stage III and IV.
- ▶ Charlson Age Comorbidity Index (CACI): the original Charlson Comorbidity Index (CCI) plus one point per age decade from 50 years and upwards. The scores were cumulated from 10 years to 90 days before the date of surgery.

TABLE 1

Regional and national data on patients undergoing pancreaticoduodenectomy for malignancies.

	Regional, unit no.				National
	1	2	3	4	
Volume 2011-2015, cases	253	121	46	56	476
Average annual production, patients	56	27	10	12	106 ^a
<i>Length of stay, days (median)</i>					
Surgical	14.1 (12)	13.9 (10)	17.2 (14)	16.6 (14)	14.6 (2)
Total	17.1 (14)	17.7 (12)	18.2 (14)	17.3 (14)	17.4 (14)
<i>Complex admission^b</i>					
Rate, %	16.6	43.0	13.0	5.4	21.6
Subsequent length of stay, days	18.3	9.0	7.5	13.0	12.8
<i>Readmissions</i>					
Total rate, %	27.6	23.3	31.8	23.1	26.4
<i>Mortality rate, %</i>					
Hospital	1.2	4.1	4.3	7.1	2.9
30-day	2.0	3.3	4.3	3.6	2.7
90-day	3.6	5.8	6.5	7.2	4.8
180-day	10.3	10.8	8.7	12.6	10.5
1-yr	24.9	29.8	37.0	25.1	27.3
<i>TNM rate, %</i>					
Preoperative:					
Indicated, any stage	20.9	54.5	8.7	19.6	28.2
Post-operative:					
No stage	2.4	3.3	13.0	0.0	3.6
Stage I	9.5	19.0	21.8	5.4	12.5
Stage II	75.5	70.2	63.0	89.3	74.5
Stage III	6.7	5.8	2.2	3.6	5.6
Stage IV	5.9	1.7	0.0	1.7	3.8
<i>Disease stage, rate, %</i>					
Burden of disease	12.6	7.4	2.2	5.4	9.5
Gender, males, %	51	51	54	57	52
<i>Age & co-morbidity</i>					
CACI (median)	3.0 (3)	2.9 (3)	2.7 (3)	2.6 (3)	2.9 (3)
CCI +3 ^c , rate, %	9.1	7.4	4.3	7.1	8.0

CACI = Charlson Age Comorbidity Index; CCI = Charlson Comorbidity Index; TNM = tumour-node-metastasis.

a) Accumulation does not match due to rounding up.

b) The patient is transferred to another unit/hospital.

c) 70-79-yr-olds.

All indicators were calculated for all of the included pancreatic procedures in total and for PD separately.

Trial registration: not relevant.

RESULTS

A total of 691 patients underwent surgery during the study period (from 1 January 2011 to 30 June 2015) with a male to female ratio of 52:48. Of these, 476 (68.9%) were treated with PD, 126 (18.2%) with total pancreaticoduodenal resection, 85 (12.3%) with distal pancreaticoduodenal resection and 4 (0.6%) with local pancreaticoduodenal resection; the latter only in one unit. No patient received more than one of the four procedures.

Further analysis is focused on PD exclusively.

Volume varied within the four units (**Table 1**). The two most productive units (1 and 2) accounted for 374 (79%) of the procedures. The average annual production in Denmark was 106 patients (range 10 - 56 per unit). There was an increase in volume for all units during the observation period.

Mean length of stay after PD was 14.6 days (median 12 days) at the performing surgical unit, but 17.4 days (median 14 days) when including all transfers. The surgical mean varied between the hospitals by 3.4 days (range 13.9 – 17.2 days). Of 476 hospitalisations, 103 (21.6%) were complex with considerable variation between the units (range: 5.4 - 43.0%). On average, patients spent 12.8 days at the receiving unit after transfer.

Readmissions within 30 days from discharge occurred a total of 122 times (26.4%) and with some variation between the units (range: 23.1 - 31.8%).

Hospital mortality included no deaths during surgery, but 14 patients (2.9%, range: 1.2 - 7.1%) died before discharge. 30-day mortality showed that 13 patients (2.7%, range: 2.0 - 4.3%) died within a month, 90-day mortality included 23 patients (4.8%, range: 3.6 - 7.2%), 180-day mortality 50 patients (10.5%, range: 8.7 - 12.6%) and one-year mortality 130 patients (27.3%, range: 24.9 - 37.0%).

See **Figure 1** for one-year survival follow-up.

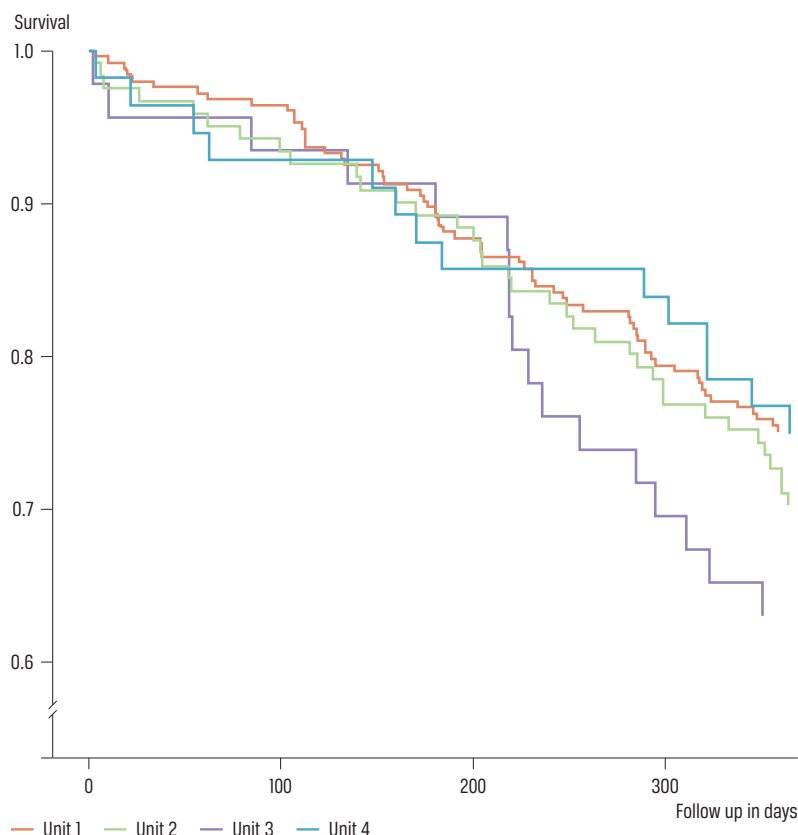
Data on DS were available for all patients (476). The preoperative stage was stated for 134 patients (28.2%, range: 8.7 - 54.5%). Postoperative staging was stated for 459 patients (96.4%) with less variation between the units (range: 87.0 - 100.0%). A majority of 355 patients (74.5%) were in disease stage II. The BOD varied more than fivefold between the units with the highest and lowest score (range 2.2 - 12.6%). Data on age and co-morbidity were obtained for all patients, and the mean CACI was 2.9, with almost no variation across the units.

All indicators were also calculated for pancreatic



FIGURE 1

Kaplan-Meier follow-up until one-year survival for each of the four units.



surgery overall (all included procedures) with results very similar to those for PD.

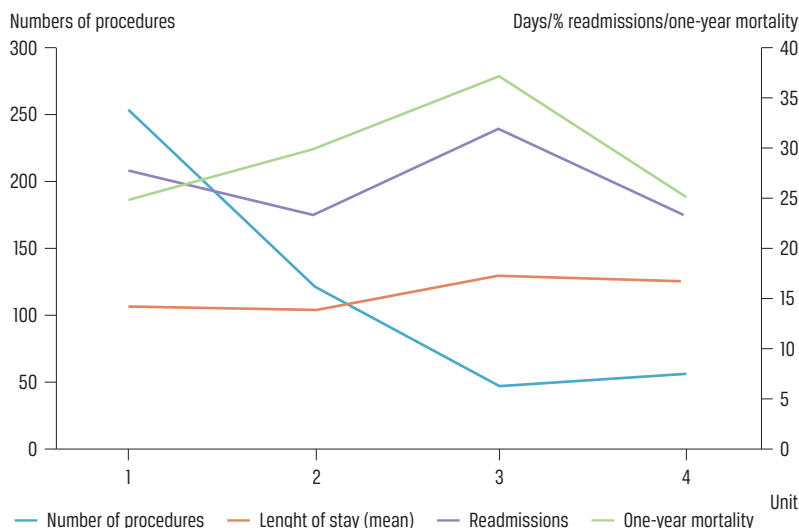
DISCUSSION

This study includes all pancreatic surgery on pancreatic cancers in Denmark from 2011 through to the first half of 2015 as registered in the DNPR. Compared with previous Danish studies on PD, the national annual production volume on malignant indication has increased from 56 patients in 1996-2001 [3], to 74 patients in 2005-2008 [4] and 106 patients in our study period. The increase in national production is possibly a consequence of the rise in incidence as well as progression in surgical skills and knowledge. Although the centralisation of cancer surgery over the past two decades has reduced the number of performing units, it has not led to an even distribution in production volume. Currently, almost 80% of the procedures is performed in two of the four units, with one unit accounting for more than 50% of all operations in Denmark.

The median length of stay has declined from 22 days in 1996-2001 [3], to 17 days in 2005-2008 [4] and 12 days in this study period. The rate of complex

 **FIGURE 2**

Volume, length of stay, readmissions, and one-year-mortality for PD at each of the performing units. Volume is specified on the primary y-axis and mean length-of-stay (surgical), readmissions, and one-year-mortality is specified on the secondary y-axis.



admissions varied considerably between the units (range: 5.4 - 43.0%), but it is unknown whether transfers were planned or acute. Regardless hereof, these situations present a potential threat to patient safety because hand-overs - whether temporary or permanent, are a complicated process which often requires a high level of awareness and preparedness within communication, information, responsibility and organisation [5]. To our knowledge, complex admission rates have not been reported in previous Danish or international studies of this kind. Readmission rates were remarkably higher in this study than previous national findings ranging from 10% in 1996-2001 [3], 11% in 2005-2008 [4] to 26.4% in the present study. It remains unknown whether this is linked to the observed decline in length of stay or complex admissions. Compared with international findings, length of stay [6-12] and readmission rates [10, 13] are roughly on a par, although data on readmission rates are sparse.

In Denmark, hospital mortality following PD on cancer has declined considerably from 11.3% in 1996-2001 [3] to 6.0% in 2005-2008 [4], and the presently recorded 2.9%. This national average is at the low end of internationally reported rates [6, 7, 12-16], thereby matching the performance of high-volume centres. Hospital mortality varied the most within the studied mortality indicators. The specifics about this are unknown, but international observations suggest that some of these types of deaths are potentially preventable [17]. Causality cannot be inferred from this study, but is most likely multifactorial. The phenomenon "failure-to-rescue" - the challenge to intervene sufficiently

towards postoperative complications - could be a contributor to this [17], but this cannot be evaluated in the present study. 30-day mortality declined from 5.9% in 1996-2001 [3] to 2.7% at present. The remaining mortality indicators revealed little variation between the units except for one-year mortality, which also showed some variation. Previous national data on this indicator do not exist, but compared with international observations, the current national average is at the low end [6, 12]. Direct comparison with earlier national findings should be interpreted with some caution as these studies include approximately 10% of patients with benign conditions as well.

The burden of disease varied between the units. This variation has also been documented by the Danish Pancreatic Cancer Database (DPCD). Arterial resections are performed only in one unit, thus treating the more advanced cancers. However, this cannot fully explain the observed difference. The TNM classification has changed during the study period, and this could influence the reported tumour stages. A potential problem has been a non-standardised evaluation of the resected specimen, which could affect the accuracy of the TNM staging and margin evaluation between units. As a consequence, the DPCG has implemented a national standardised pathology protocol, which will hopefully align the TNM classification nationwide.

Overall, the population-based resection rate in Denmark is on a par with international levels [18], but the absolute number of annual PDs in Denmark is low. The uneven distribution of the production volume divides the four existing units into two high- and two low-volume units. The link between volume and mortality - both in the short and long term - has not been firmly established in this study (see **Figure 2**), but multicentre studies on pancreatic surgery have found a positive association between a high resection volume and a low mortality [7, 14, 16-19]. Internationally, long-term mortality has been associated with a high tumour grade [20], in this study the reverse association was suggested for one unit where a low tumour grade was associated with the highest one-year mortality.

CONCLUSIONS

This study suggests that a need exists for identification of factors potentially contributing to the observed variations in complex admissions, readmissions and, especially, mortality. Thus, further studies on the link between mortality, volume and BOD are required.

The aim of this study was to uncover any regional variations in surgical outcomes across the four producing units. The inequity in the number of patients in some units (i.e., those with a very small numbers of patients) impedes rigorous statistical analysis.

The identified variations illustrate a potential dis-

parity across the country, which might indicate that a safety gap exists and future follow-up data are required to determine causality.

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